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ORIGINAL ARTICLE

Is there a correlation between the carotid intima media thickness (CIMT) and the coronary artery calcium score (CACS) as predictors of atherosclerotic cardiovascular disease (ASCVD)?

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ABSTRACT

Background: Coronary artery calcium score (CACS) and carotid intima-media thickness (CIMT) are important markers for early detection of coronary atherosclerosis. The study aimed to investigate the relationship between the CIMT and the CACS as markers for atherosclerotic coronary artery disease (CAD).

Methods: This single-center prospective study enrolled 41 cases with suspected CAD. The cases underwent carotid artery US and CA non-contrast CT (NCCT). A radiologist with eight years of experience in vascular US imaging performed the carotid artery US, while two radiologists with ten years of experience in cardiac imaging analyzed the coronary artery CT images and assigned a CAC-DRS category for each case. We used the Pearson correlation test to calculate the correlation between CIMT and CACS. The receiver operating characteristics (ROC) curve was used to estimate the best cutoff value of CIMT in predicting CA heavy calcification.

Results: The study included 41 cases of suspected CAD, of which 12-showed heavy, and 29 showed non-heavy CA calcification. The mean CACS was 163, and the highest CIMT was 0.785 mm among the included patients. There was a significant positive correlation between the CACS and the highest CIMT (r 0.606 and P <0.001). A CIMT > 0.8 mm was the best cutoff for predicting heavy calcification, with a sensitivity of 91.7%, a specificity of 65.5%, and an accuracy of 73.2% based on ROC curve analysis.

Conclusions: CIMT and CACS can be considered non-invasive predictive measures for CA atherosclerosis and subsequent CAD. Moreover, these markers might help cardiologists in clinical management.

Keywords: Coronary calcium; Coronary artery disease; Carotid artery; Atherosclerosis

INTRODUCTION

Atherosclerosis is known as a process of accumulation of lipids, fibrous components, and calcification inside the major arteries. Endothelium activation begins this process, followed by a series of actions that reveal vessel narrowing and induction of inflammatory pathways that result in the creation of atheromatous plaque. When paired together, all of these factors contribute to cardiovascular problems, which continue to be the world's leading cause of mortality. [1].

Various lifestyle factors have been linked to the development of atherosclerosis, such as high blood levels of LDL and cholesterol, low blood levels of HDL (high-density lipoprotein), tobacco smoke, hypertension

(HPN), diabetes mellitus (DM), and obesity. [2].

Atherosclerosis is a slowly developing condition that affects blood vessels throughout life. It can begin in childhood and worsen with age. Thus, before complete full-clinical disorders such as coronary artery disease (CAD), stroke, and peripheral artery disease (PAD) develop, atherosclerosis has a prolonged latent phase. [3].

According to earlier research, clinical symptoms of atherosclerosis are typically associated with an advanced stage; beyond this point, medical therapies have little effect. Atherosclerosis causes significant alterations in the affected arteries before the onset of clinical symptoms, including endothelial dysfunction, thicker intima-media, and arterial calcification. As a result, these changes may serve as indicators for an early atherosclerosis diagnosis. [4]**.**

A specific type of computed tomography (CT) scan of the heart is called a coronary artery calcium scan. Automated software shows calcium deposits in the coronary arteries (Agatston method). Calcium accumulation over time may cause artery narrowing and decreased cardiac blood flow. Before the onset of clinical symptoms, coronary artery disease (CAD) may be predicted by the coronary artery calcium score (CACS). CACS is useful in assessing a high-risk patient's risk of heart attacks or strokes. As a result, CACS may be used to plan or change CAD treatment. As a way to evaluate the patency of the coronary artery lumen, coronary CT angiography (CCTA) uses the CACS as a screening technique. [5]**.**

The measurement of the combined thickness of the carotid artery's intima and media layers is known as carotid intima-media thickness (CIMT), and it is generally measured by B-mode ultrasonography. Since cellular or molecular pathways that raise CIMT are also responsible for the development and progression of atherosclerosis, an increase in CIMT may result from hypertrophy of either the medial or intimal layers or both. [6].

CIMT is considered to be a good indicator of asymptomatic and subclinical atherosclerosis. There is evidence that the degree and severity of atherosclerosis in many vascular systems throughout the body are correlated with atherosclerotic lesions in the common carotid artery (CCA). [6].

The American Heart Association accepts CIMT and CACS as stand-in markers for coronary artery disease. Compared to CACS (measured by coronary CT scan), CIMT (measured by B-mode ultrasonography) has the benefit of not requiring ionizing radiation, being less expensive, easy to perform, and capable of detecting illness among individuals who are asymptomatic and young. CIMT could, therefore, predict the degree of CAD. In addition, IMT increased in individuals with more advanced CAD. **[7].**This study aimed to determine the correlation between the CACS and CIMT as predictors for atherosclerosis. As a secondary aim, the optimal cutoff CIMT value for predicting heavy calcification was estimated.

METHODS

Study design and population

This prospective single-center study recruited 49 consecutive patients between April 2023 and December 2023. They were referred from the cardiology Department to the Radiodiagnosis Department. Prior to the start of the study, we obtained approval from the local institutional review board (IRB) with a reference number (No: 10674). Informed consent was obtained from all participants. We followed the Declaration of Helsinki's concepts and the STROBE guidelines for reporting a cross-sectional study [8].

Inclusion criteria were (i) Adult patients of both sexes; (ii) Patients who were suspected of having CAD and complaining of typical or atypical chest pain; (iii) Patients with risk factors for atherosclerosis such as DM, HPN, and smoking.Exclusion criteria were (i) Patients with previous CABG or PCI (n=3); (ii) Patients with recent myocardial infarction (n=1); (iii) Congenital heart diseases (n=2); (iv) Pregnant cases (n=1); (v) Suboptimal CT or US images (n=1).

Forty-one patients (14 females and 27 males) met our eligibility criteria. Patients' basic characteristics are summarized in **(Table 1)**.

All patients underwent detailed history taking, a comprehensive clinical assessment (general and cardiological), and laboratory tests such as lipid profiles. Coronary arteries NCCT scan and carotid artery US were performed for all eligible patients.

Technique of coronary arteries NCCT scan

Patient preparation

A B-blocker (metoprolol) 50 mg was given for every patient one hour before the exam except if there was a contraindication, ivabradine was given instead, fasting for one hour prior to the scan is advisable, and sedation was needed for some patients.

Scan protocol and parameters

A 160-slice dual-source CT scanner (Canon medical system incorporation, aquilion prime sp, tsx-303b, Japan) was utilized. A scano-gram was obtained from the level of the carina to the base of the heart. Image acquisition was performed using a retrospective ECG gating using the following parameters: automated adjusted Tube current in mA, Tube voltage 100-120 KV, slice thickness of 2.5 mm, and gantry rotation time of 280 ms.

Image interpretation and analysis

An updated workstation received all CT data. Two radiologists with ten years of experience in cardiac imaging who were blinded to the clinical data assessed and analyzed all CT images in consensus. CACS was estimated by automated software using the Agatston method [9]. Any lesion with an area of >1 mm^2 and with a density > 130 HU was colored and marked, then an automatic calculation of CACS was done. Finally, the CAC-DRS category [10] was assigned for each patient.

Technique of carotid artery US

All examinations were performed by a radiologist with 8-years experience in vascular US imaging using a General Electric GE Logiq P7 scanner (GE Medical Systems, Waukesha, USA®) with a high frequency (4-12 MHz) linear transducer. The examination was done with the patient lying in a supine position, his neck slightly hyperextended and turned towards the opposite side of the examined side.

All vessels were scanned in transverse and longitudinal planes using grey scale, color Doppler, and spectral Doppler.

One to two centimeters before the carotid bifurcation at the distal wall of the common carotid artery, the CIMT was calculated for the RT and LT CCAs in the longitudinal àxis. On each side, two measurements were obtained, and the average was calculated. There are qualitative (visual) and quantitative approaches used to analyze carotid plaques. It is necessary to perform a circumferential scan from anterior to posterior angles, imaging the internal carotid artery segments, bulb, and near or far wall of the common carotid artery. A plaque long axis evaluation is used to confirm its maximum size if it is observed from an axis perspective. The plaque was identified as a localized wall thickening more than 50% of the adjacent IMT or a CIMT greater than 1.5 mm. The following parameters were identified for each plaque: location, number, length, irregularity (smooth, irregular, or ulcerated), and echogenicity (echogenic, mixed echogenic, or echo lucent). Then, we performed a correlation analysis between the CACS and CIMT using the appropriate statistical tests. Moreover, we used the ROC curve to calculate the best CIMT cutoff for predicting heavy calcification [9].

STATISTICAL ANALYSIS

The data were collected and statistically analyzed using SPSS 22.0 for Windows (IBM Corp., Armonk, NY, USA). Continuous data were expressed as the mean ± SD or median (IQR) regarding normal or abnormal distribution by the test of normality (Shapiro-Wilk test), while categorical data were expressed as numbers and frequencies (percentage). The chi-square for the trend test was used to compare ordinal categorical data. The correlation was estimated using Pearson's correlation coefficient tests when appropriate and presented as r and p values. The strength of the relationship between CAC-DRS and carotid IMT was determined by computing Kendall's tau-c correlation coefficient. The receiver operating characteristic (ROC) curve was utilized to estimate the cutoff value and the area under the curve (AUC) of CIMT for predicting heavy calcification. P-value< 0.05 was considered statistically significant (S), and p-value < 0.001 was considered highly statistically significant (HS).

RESULTS

This study included 41 patients (27 males and 14 females) with suspected CAD. The mean age of the studied cohort was 52.39 ±9.1 years. Twelve cases showed heavy, and 29 showed non-heavy coronary artery calcification. The mean of CACS was 163.59±198.19, and of CIMT was 0.785±0.287 mm, as shown in **(Table 1).**

CAC-DRS categories assignment by both readers

CAC-DRS categories, according to the readers, are summarized in **(Table 2).** The most frequently reported categories were CAC-DRS 1 (34.1%), followed by CAC-DRS 3 (29.3%) and CAC-DRS 0 (22%).

Association and correlation between CAC-DRS categories and CIMT (with CIMT < 0.8 was considered as a normal reference value)

There was a significant association and correlation between CAC-DRS categories and CIMT (X^2 =21.81, P<0.001 and r=0.849, P <0.001), respectively. The association and correlation between CAC-DRS and CIMT is described in **(Table 2).**

Correlation between CACS and CIMT

As shown in **(Table 3) and (Figure. S1)**, there was a significant positive correlation between the CACS and the CIMT (r=0.606, P <0.001)**.**

Analysis of the ROC curve

ROC curve analysis was utilized to calculate the cutoff value of CIMT to predict heavy coronary artery calcification **(Figure. 1)**. CIMT > 0.8 mm was the best cutoff value in predicting CAC-DRS 3 with a sensitivity, specificity, and accuracy of 91.7%, 65.5%, and 73.2%, respectively with an AUC of 0.774, (**Table 4).Cases are illustrated in (Figures. 2 and 3) and (Figure. S2).**

Table 1: Basic Demographic, clinical Characteristics, Coronary NCCT, and Carotid artery US findings of the studied patients (N=41).

Basic Characteristics	**The studied patients (N=41)**	
	Number	**Percent**
Sex		
Male	27	65.9%
Female	14	34.1%
Age (years)		
Mean±SD	52.39	±9.10
Median (Range)	55	(35 – 68)
Risk factors		
Current smoker	9	22%
Diabetes	25	61%
Hypertension	22	53.7%
Hyperlipidemia	14	34.1%
Obesity	38	72.7%
Family history of premature CAD	7	17.1%
Clinical presentation		

Basic Characteristics	The studied patients (N=41)	
	Number	**Percent**
Typical Chest pain	31	75.6%
Atypical Chest pain	10	24.4%
Dyspnea	31	75.6%
Syncope	4	9.8%
ECG findings		
Non-specific	31	75.5%
Specific	10	24.4%
Depression ST segment	9	22%
T wave changes	6	14.6%
Cardiac enzymes		
Normal	41	100%
Abnormal	0	0%
Median (Range)	50	(0 – 836)
Calcium score grading		
No (0)	9	22%
Minimal (1-10)	2	4.9%
Mild (11-100)	13	31.7%
Moderate (101-400)	12	29.3%
Severe (>400)	5	12.2%
CAC-DRS Calcium score		
CAC-DRS 0 (0)	9	22%
CAC-DRS1 (1-99)	14	34.1%
CAC-DRS 2 (100-299)	6	14.6%
CAC-DRS 3 (>300)	12	29.3%
Degree of CA calcification		
Heavy calcification	12	29.3%
Non-heavy calcification	29	70.7%
Right IMT (mm)		
Mean±SD	0.658	±0.262
Median (Range)	0.6	(0.3 – 1.2)
Left IMT (mm)		
Mean±SD	0.722	±0.287
Median (Range)	0.6	(0.3 – 1.4)
Highest IMT (mm)		
Mean±SD	0.785	±0.287
Median (Range)	0.8	(0.3 – 1.4)
Right plaque		
Absent	26	63.4%
Present	5	36.6%
Left plaque		
Absent	24	58.2%

Basic Characteristics	**The studied patients (N=41)**	
	Number	**Percent**
Present	17	41.5%

Categorical variables were expressed as numbers (percentages).
Continuous variables were expressed as mean ± SD & median (range).

Table 2: Association and Correlation between CIMT and CAC-DRS among the studied patients (N=41).

CAC-DRS		**CIMT**		**Total**
		CIMT ≤ 0.8 mm	**CIMT > 0.8 mm**	
CAC-DRS 0	No.	9	1	10
	(%)	(21.95%)	(2.44%)	(30.8%)
CAC-DRS 1	No.	10	3	13
	(%)	(24.39%)	(7.32%)	(32.7%)
CAC-DRS 2	No.	1	5	6
	(%)	(2.44%)	(12.2%)	(25%)
CAC-DRS 3	No.	2	10	12
	(%)	(4.88%)	(24.39%)	(11.5%)
Total	No.	22	19	41

Association		**Correlation**	
Test[a]	p-value (Sig.)	Coefficient	p-value (Sig.)
17.51	<0.001 (HS)	+0.690	<0.001 (HS)

Categorical variables were expressed as numbers (percentage); a: Chi-square for trend test; b: Kendall's tau-c; p-value < 0.05 is significant; Sig.: Significance.

Table (3): Correlation between the highest carotid artery IMT and Ca score among the studied patients (N=41).

Correlation		**NCCT**	**Total**
		Ca Score	
Highest carotid IMT (mm)	**Coefficient (r)**	**+0.606[a]**	**41**
	p-value	**<0.001 (HS)**	**(100%)**

a: Pearson correlation test; p-value < 0.05 is significant; Sig.: Significance.

Table (4): Validity of CIMT for prediction of heavy calcification (N=41).

Variables	AUC	95%CI	Cutoff	Sensitivity	Specificity	PPV	NPV	Accuracy
CIMT	0.774	0.614-0.934	> 0.80	91.7%	65.5%	52.4%	95%	73.2%

AUC: area under curve; PPV: positive predictive value; NPP: negative predictive value.

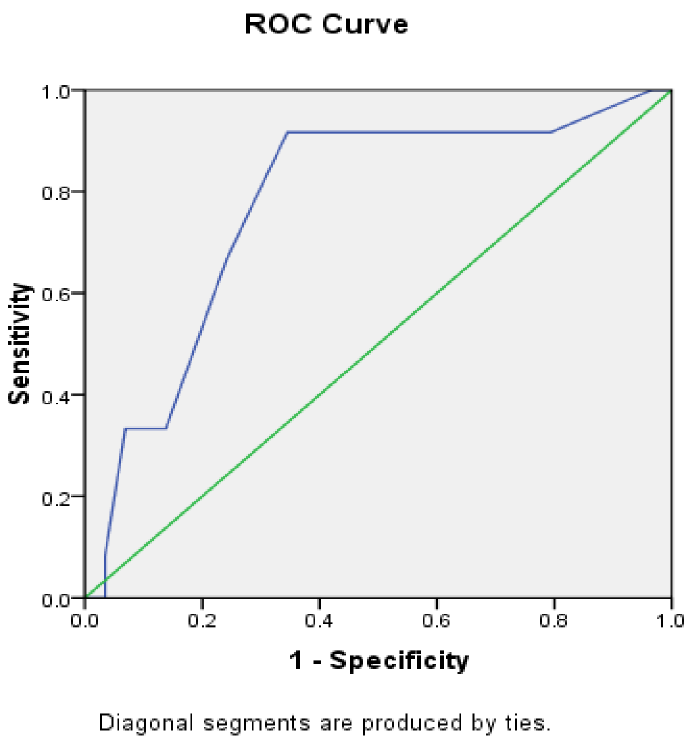
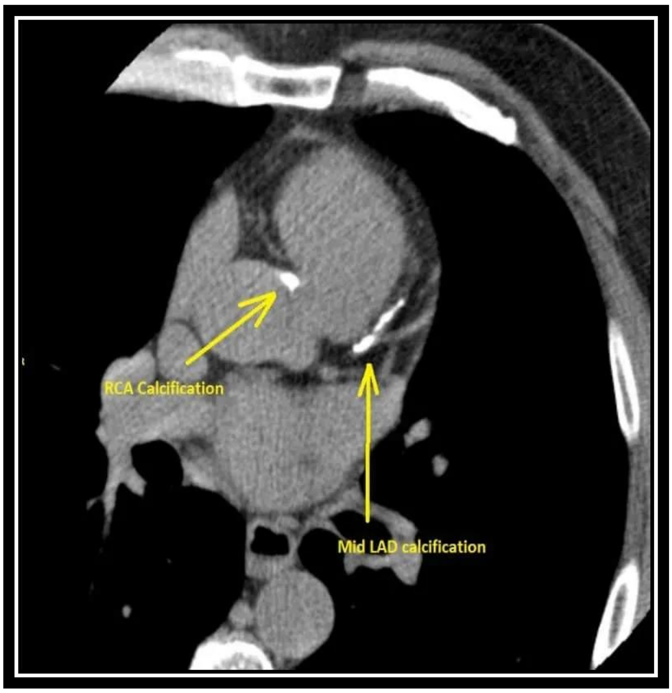
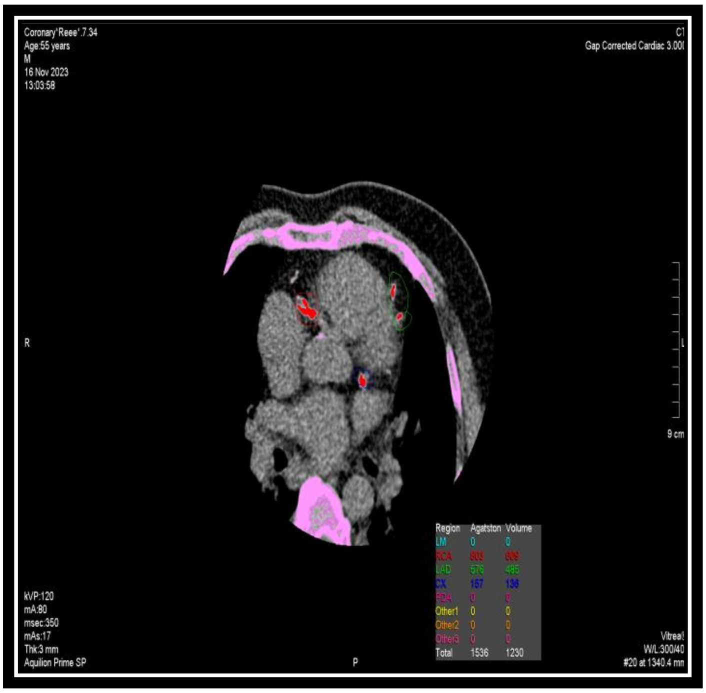


Figure. 1: ROC curve of the carotid artery IMT (CIMT) for prediction of coronary artery heavy calcification.



(A)



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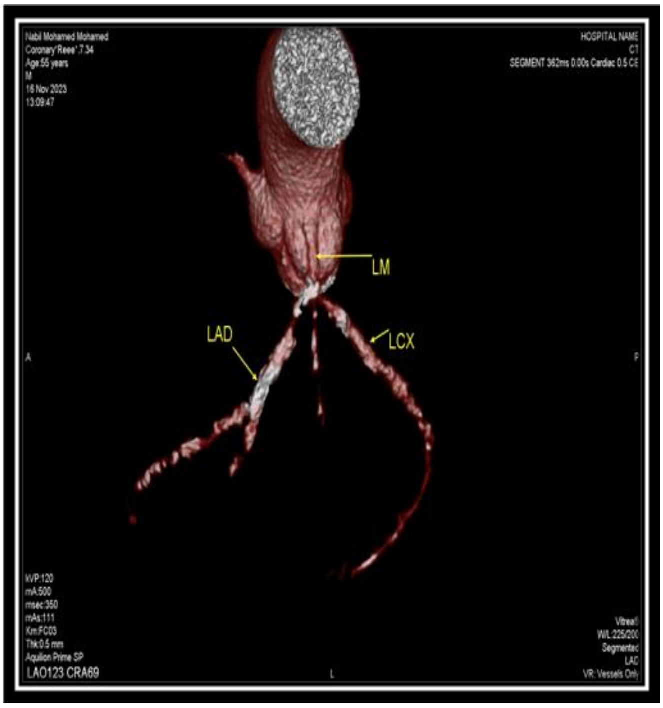

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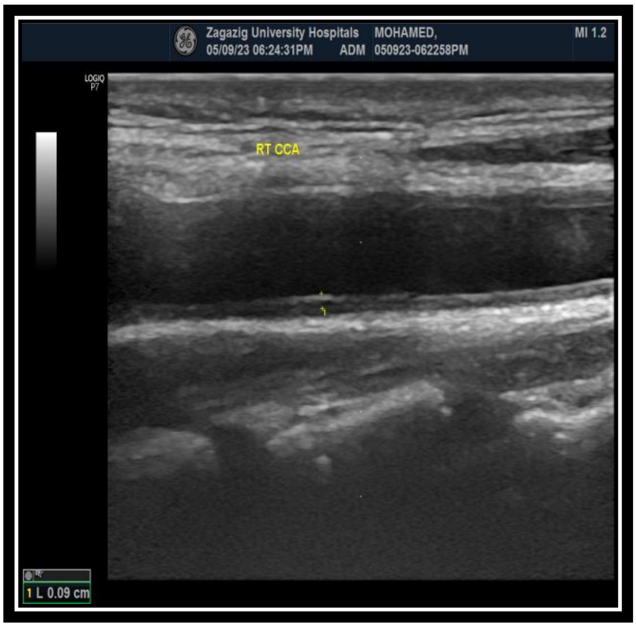
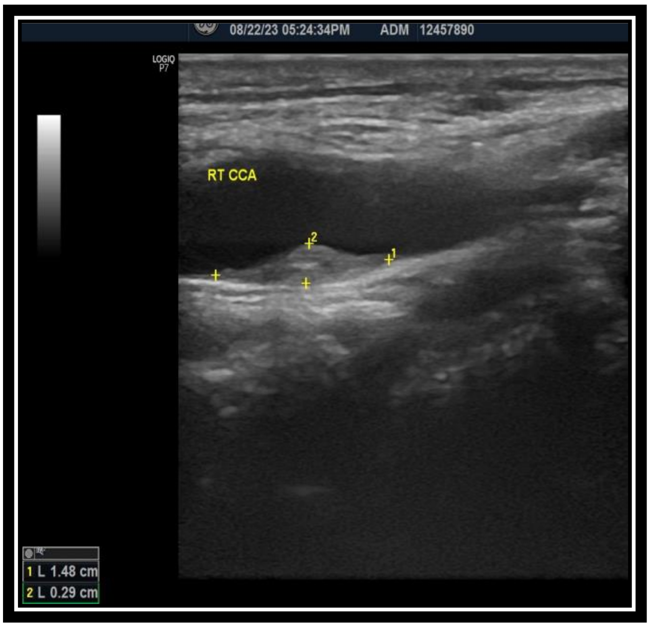
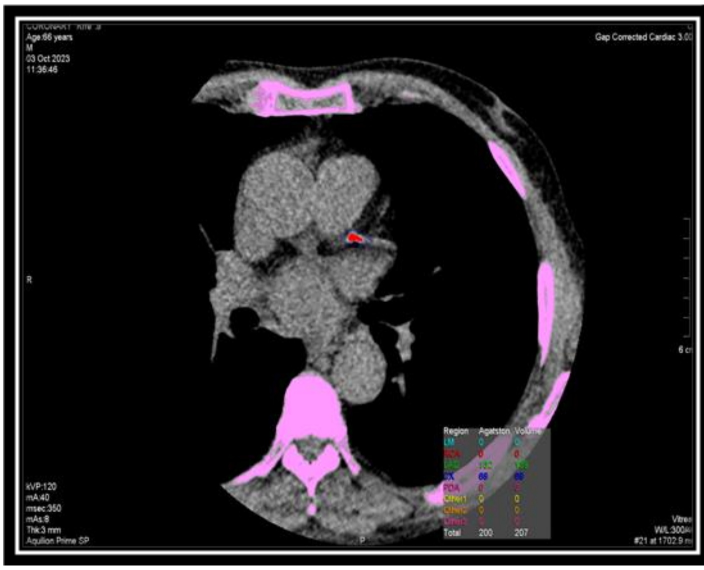
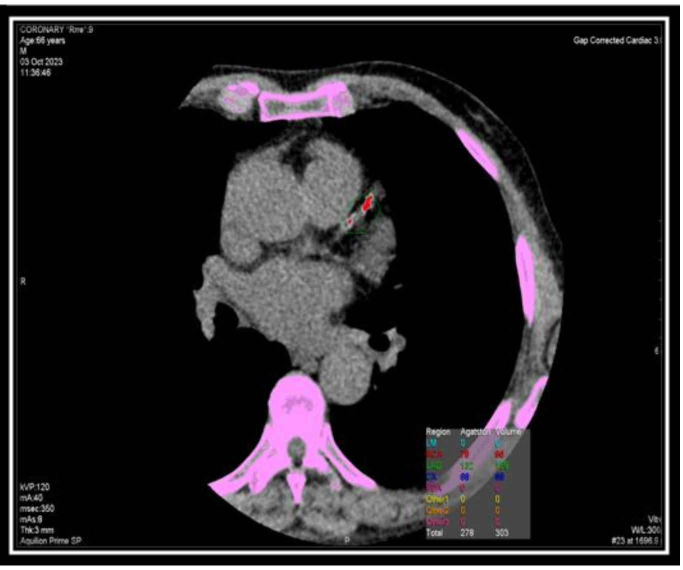


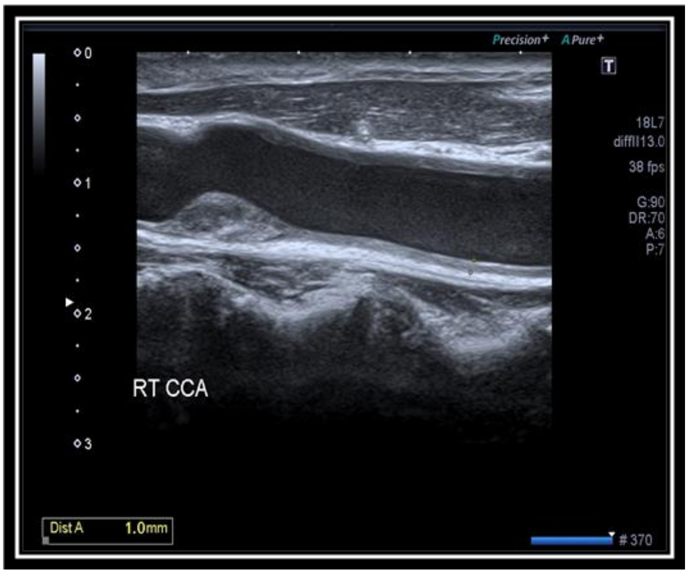


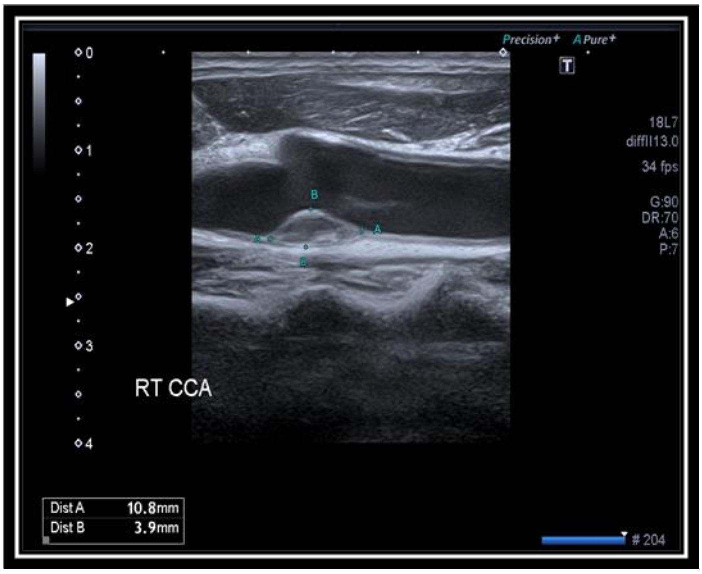
(D) **(E)**

Figure. 2: A 65-years old hypertensive male patient complained of typical chest pain. (A) and (B) Axial sections of non-contrast CT (NCCT) scan of the coronary arteries show left and right coronary calcification with Agatston Ca score of 1536. (C) 3D volume rendered image of the left coronary artery tree show heavy coronary calcification. (D) and (E) Longitudinal US images of RT CCA show CIMT of 0.9 mm associated with mixed atheromatous plaque 15x3 mm. The patient was assigned as CAC-DRS 3.

(A) (B)





(C) (D)

Figure. 3: A 60-years old diabetic male patient, complained of recurrent attacks of chest pain. (A) Axial section of non-contrast CT (NCCT) scan of the coronary arteries shows Agatston Ca score of 200. (B) and (C) Longitudinal US images of the RT CCA demonstrate thickened CIMT measuring 1 mm with mixed atheromatous plaque exerting significant stenosis up to 70%. The patient was assigned as CAC-DRS 2.

DISCUSSION

Clinical significance

The current study is an attempt to provide the literature on the clinical impact of the early detection of subclinical and early stages of atherosclerosis for better clinical management of high-risk patients of CAD [11]. CACS and CIMT are considered surrogate predictive markers for coronary artery atherosclerosis and subsequent cardiovascular events. Therefore, these markers might be used as screening tools for CAD development [12].

Coronary artery calcification is a late process of atherosclerosis, while increased CIMT is an early indicator of it. Therefore, CIMT is considered more sensitive for early detection of CAD in high-risk individuals. Both markers can provide crucial information for risk stratification and be used as prognostic tools for the extent of CAD [13].

Summary and explanation of the results

Our study provided evidence about the relation between the CIMT and CACS for predicting further coronary artery atherosclerosis and subsequent CAD. The current study included 12 patients with heavy (CAC-DRS 3) and 29 patients with non-heavy (CAC-DRS <3) coronary artery calcification. The mean of the CACS was 163.59±198.19, and the highest CIMT was 0.785±0.287 mm among the included patients. Moreover, there was a significant positive correlation between the CACS and the highest CIMT (r 0.606 and P <0.001). Furthermore, there was a significant correlation and association between CAC-DRS categories and CIMT (P <0.001). These findings were not surprising and could be explained by the fact that CACS and CIMT are investigated in previous reports [14,15] as robust imaging tools for assessing subclinical and early atherosclerosis. The optimal cutoff value of CIMT for predicting heavy calcification was > 0.8 mm with sensitivity and specificity of 91.7 and 65.5%, respectively.

Agreement and disagreement with the previous literature

To the best of our knowledge, a paucity of studies investigated the relation between CACS and CIMT and assessed which marker is sensitive for predicting CAD. However, many studies [16, 17] assessed the correlation between these markers and the severity of CAD.

Greshma et al. [14] reported a mean CACS of (135 V 163) and a mean CIMT of (0.5 v 0.785) mm among their included cohort. This is partially in agreement with our study. This might be attributed to the different devices, races, and experiences of the raters. Moreover, Greshma et al. [14] investigated the correlation between CIMT and CACS. They found a positive significant correlation between both markers in line with our study (r = 0.450, P = 0.001 v r=0.606, P <0.001). In addition, they reported a significant association between CACS grading and CIMT (P <0.005). This is in line with our report despite using different CIMT cutoff values for normal references. Another team in the United States [13] reported that patients with higher CACS showed an increased CIMT, which is in accordance with our findings. In line with our findings, a relevant study [18] that investigated the correlation between the CIMT and the European Society cardiology score, reported a significant correlation between the increased CIMT and the cardiovascular risk score. Furthermore, Estrada et al. [19] study revealed a significant correlation between increasing the CIMT and increasing the cardiovascular risk in the form of atherosclerosis and subsequent ischemic heart disease. Our results and the previously conducted studies prove the significant relation between both markers, and any of them can be used as a non-invasive screening tool for early atherosclerosis. Thus, better preventive measures for subsequent cardiovascular events can be initiated.

To our knowledge, few studies assessed the best cutoff of CIMT in predicting heavy calcification or high CACS. On ROC curve analysis, CIMT > 0.8 was the optimal cutoff value for predicting CAC-DRS 3. In line with our findings, Outsuka et al. [20] reported a

CIMT ≥ 0.83 mm as an optimal cutoff value for predicting heavy calcification. However, no other comparable reports showed a relevant cutoff value. Therefore, we recommend conducting future prospective studies to confirm or contradict the current findings.

Based on the current study, the CIMT can be considered a sensitive marker for subclinical atherosclerosis and positively correlated with CACS. It is simple, applicable, and available. However, it has a few drawbacks because some patients with CACS zero showed an increased CIMT. This can be explained by the fact that CAC is a late process in atherosclerosis, and the patients might show coronary non-calcified fatty or fibrous plaques that may induce obstructive CAD with no significant detected CAC. To enhance its preventive role, we recommend conducting similar studies on asymptomatic high-risk subjects for better risk stratification.

Clinical implications

CIMT and CACS can be used in clinical practice as non-invasive and available imaging tools for evaluating coronary artery atherosclerosis. Furthermore, it reduces the use of aggressive interventions and promotes initiating early preventive measures for CAD.

Limitations

Our study had some limitations. First, it was a single-center study with a small sample size. Second, we did not investigate the correlation between CIMT, and CACS with the presence of CAD. Therefore, further prospective multicenteric studies with a large sample size are recommended to evaluate the relation between these markers and CAD.

CONCLUSIONS

CIMT and CACS can be considered as non-invasive predictive measures for coronary artery atherosclerosis and subsequent cardiovascular events. Moreover, these markers might help clinicians in better management and improve the potential patients' outcomes.

Authors' contributions: NYE and AO have the idea of research, follow-up cases, writing, publishing, and analysis of the data. MFE and NYE have the final revision and supervision. AO and NYE refer the cases and adjust any clinical problem and patient feedback. AE meticulous aid in writing. All authors read and approved the final manuscript.

Conflict of interest: None

Financial Disclosure: None

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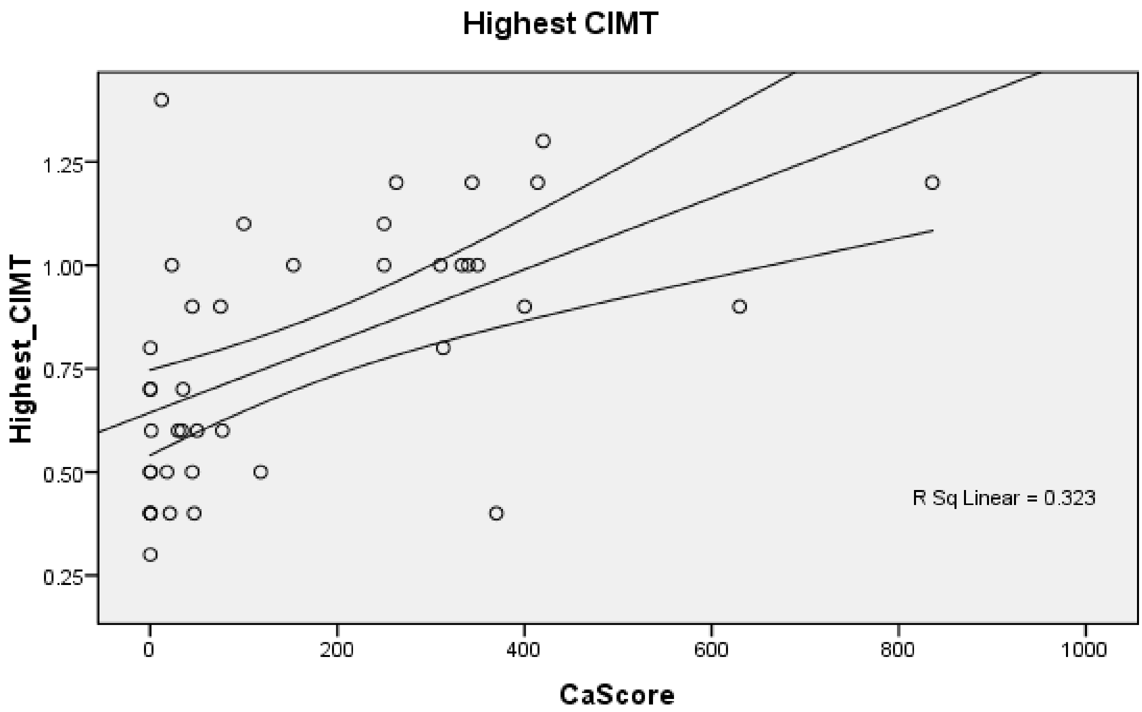
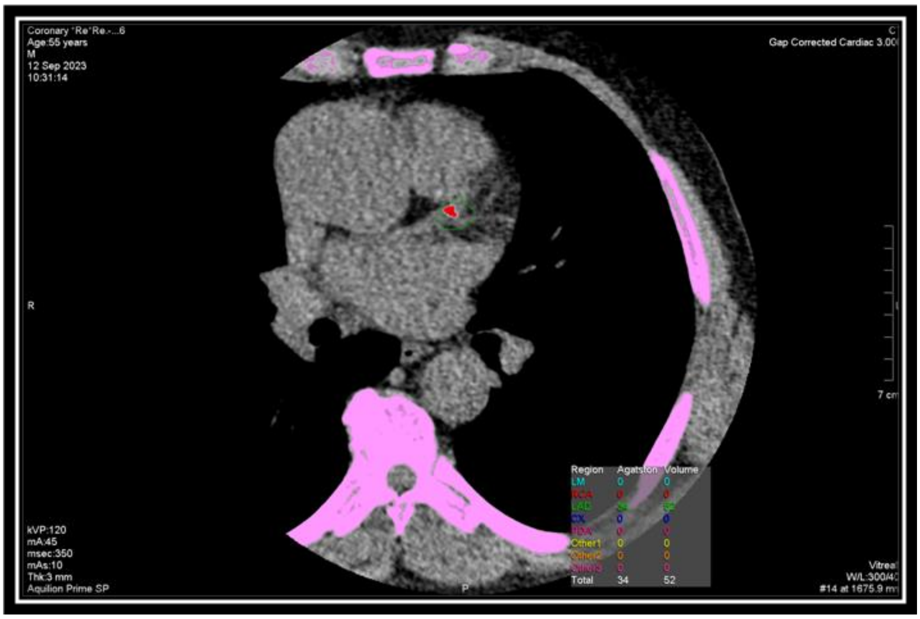
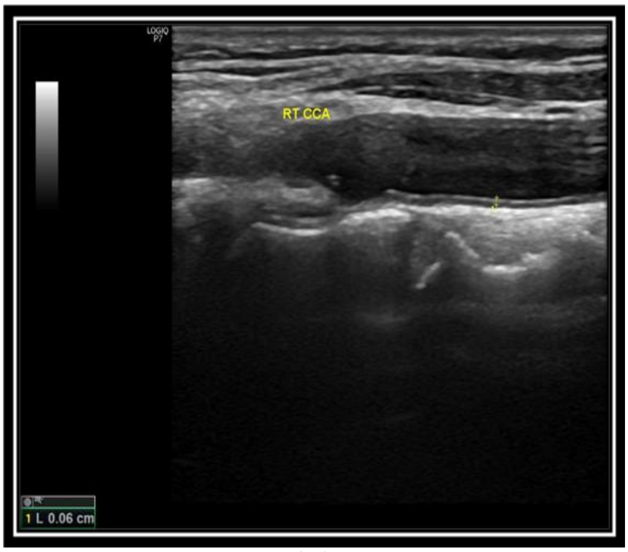


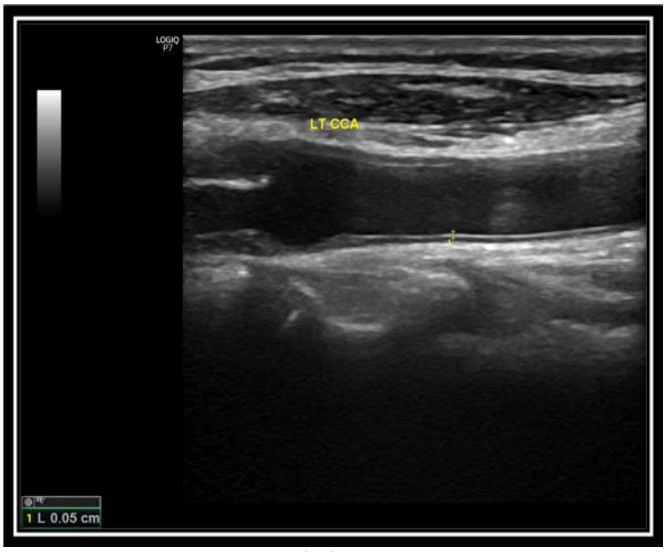
Figure. S1: Scatter plot shows the correlation between the highest CIMT and Ca score.



(A)



(B)



(C)

Figure. S2: A 58-years old hypertensive female patient complained of typical chest pain. (A) Axial section of non-contrast CT (NCCT) scan of the coronary arteries shows Agatston Ca score of 34. (B) and (C) Longitudinal US images of RT and LT CCAs show RT and LT CIMT of 0.6 and 0.5 mm, respectively. The patient was assigned as CAC-DRS 1.

Citation:

Ebaid, N. Y., Said, A. O. M., Eltohamy, M., El-Maghraby, A. M. Is there a correlation between the carotid intima-media thickness (CIMT) and the coronary artery calcium score (CACS) as predictors of atherosclerotic cardiovascular disease (ASCVD)?. *Zagazig University Medical Journal*, 2024; (3161-3174): -. doi: 10.21608/zumj.2024.265971.3143